

PATENT COOPERATION TREATY

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From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

To:
WOLF, GREENFIELD & SACKS, P.C.
Attn. Lockhart, Helen C.
600 Atlantic Avenue
Boston, Massachusetts 02210
UNITED STATES OF AMERICA

DOCKETED
FEB 20 2002

(PCT Rule 44.1)

Applicant's or agent's file reference
M0656/7064W0

Date of mailing
(day/month/year)

19/02/2002

International application No.
PCT/US 01/10249

FOR FURTHER ACTION

See paragraphs 1 and 4 below

Applicant

International filing date
(day/month/year)

30/03/2001

MASSACHUSETTS INSTITUTE OF TECHNOLOGY et al.

Subject to PTA? YES/NO
per docket/ECB

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.
Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

	Initials
File Folder	
ECB	
Docket Entry	
Docket Cross	
Order Copies	
Annulment	
Confirmation	

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority
European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Chantal Meyer

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference M0656/7064W0	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/US 01/ 10249	International filing date (day/month/year) 30/03/2001	(Earliest) Priority Date (day/month/year) 03/04/2000
Applicant MASSACHUSETTS INSTITUTE OF TECHNOLOGY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.
☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).
3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant. /
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- ☒ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☐ None of the figures.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/10249

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 A61K38/37 A61P25/28 A61P17/02 A61P35/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, MEDLINE, SCISEARCH, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 74378 A (UNIV CALIFORNIA) 11 October 2001 (2001-10-11) the whole document	1, 2, 5, 28, 29, 31-34, 37, 42-46, 48-50, 52-59, 61, 62, 65
P, X	BEAR J E ET AL: "Negative regulation of fibroblast motility by Ena/VASP proteins" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 101, no. 7, 23 June 2000 (2000-06-23), pages 717-728, XP002183154 ISSN: 0092-8674 the whole document	1-6, 8-62, 64-69, 71-75
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

24 January 2002

Date of mailing of the international search report

19/02/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

De Kok, A

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/10249

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU, K. ET AL.: "Reversible tumorigenesis induced by deficiency of vasodilator-stimulated phosphoprotein" MOLECULAR AND CELLULAR BIOLOGY., vol. 19, no. 5, May 1999 (1999-05), pages 3696-3703, XP002188207 AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON., US ISSN: 0270-7306 the whole document	17,18, 22,28, 29,59, 64,71-75
A		1,2, 8-10,14
X	GERTLER, F.B.: "Mena, a relative of VASP and Drosophila Enabled, is implicated in the control of microfilament dynamics" CELL, vol. 87, 18 October 1996 (1996-10-18), pages 227-239, XP002188208 CELL PRESS, CAMBRIDGE, NA., US ISSN: 0092-8674 page 231 page 233, column 2 -page 236, column 2	1,2,8,9, 28-32, 37,59-62
A		4-6, 13-16
X	WO 98 01755 A (BIOTECHNOLOG FORSCHUNG GMBH)) 15 January 1998 (1998-01-15)	1,2,8,9, 28,59, 64, 71-74,82
X	page 44; example 8	1,2,8,9
X	page 44, line 3 - line 12	28
X	page 29, line 3 -page 30, line 11	59,64
X	page 27, line 30 -page 28, line 6; example 11	71-75
X	page 37, line 21 - line 30	82
A	page 5, line 16 -page 9, line 13	1,13, 15-17, 25-27, 33,37, 45,52, 59,65

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>ASZODI ATTILA ET AL: "The vasodilator-stimulated phosphoprotein (VASP) is involved in cGMP- and cAMP-mediated inhibition of agonist-induced platelet aggregation, but is dispensable for smooth muscle function."</p> <p>EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 18, no. 1, 4 January 1999 (1999-01-04), pages 37-48, XP002188209 ISSN: 0261-4189 abstract</p>	1
Y	<p>HAUSER WOLFGANG ET AL: "Megakaryocyte hyperplasia and enhanced agonist-induced platelet activation in vasodilator-stimulated phosphoprotein knockout mice."</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 96, no. 14, 6 July 1999 (1999-07-06), pages 8120-8125, XP002188210 July 6, 1999 ISSN: 0027-8424 abstract page 8120, column 2</p>	1
A	<p>US 5 990 087 A (CORLEY NEIL C ET AL) 23 November 1999 (1999-11-23) cited in the application</p> <p>column 19 -column 27</p>	17-24, 33-51, 59-62, 64-69
T	<p>MACHESKY, L.M. ET AL.: "Putting on the brakes: a negative regulatory function for Ena/VASP proteins in cell migration"</p> <p>CELL, vol. 101, 23 June 2000 (2000-06-23), pages 685-688, XP002188211 CELL PRESS, CAMBRIDGE, NA., US ISSN: 0092-8674 page 685 -page 686</p>	1,37
T	<p>REINHARD M ET AL: "Actin-based motility: stop and go with Ena/VASP proteins"</p> <p>TIBS TRENDS IN BIOCHEMICAL SCIENCES, ELSEVIER PUBLICATION, CAMBRIDGE, EN, vol. 26, no. 4, 1 April 2001 (2001-04-01), pages 243-249, XP004241853 ISSN: 0968-0004</p>	1

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/10249

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>KRAUSE MATTHIAS ET AL: "Fyn-binding protein (Fyb)/SLP-76-associated protein (SLAP), Ena/vasodilator-stimulated phosphoprotein (VASP) proteins and the Arp2/3 complex link T cell receptor (TCR) signaling to the actin cytoskeleton." JOURNAL OF CELL BIOLOGY, vol. 149, no. 1, 3 April 2000 (2000-04-03), pages 181-194, XP002188277 ISSN: 0021-9525 page 192, column 1, last paragraph -column 2, paragraph 2 -----</p>	1

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Insofar as claims 1-10, 13-16, 28-33, 37, 38, 42 and 43 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds/compositions.

Although claims 12, 17-24, 34-36, 39-41, 44-58 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds/compositions.

Continuation of Box I.2

Claims Nos.: 2-6, 8, 18-22, 29, 31, 33, 34, 37-59, 65, 66 partly and 7, 63, 70, 76-81, 84 completely

Present claims 2-6, 8, 18-22, 56-58, 65, 66 relate to a method referring to the use of a compound defined by reference to a desirable characteristic or property, namely by its ability to activate Ena/VASP. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the subject-matter of claims 4-6 and 8.

Claims 7, 63, 70, 81 completely and claims 21, 31 partly have not been searched since the term peptidemimetic or mimetic has not been defined in structural terms.

Present claims 29, 33, 34, 37-50, 52-55, 59, relate to a compound defined by reference to a desirable characteristic or property, namely by its ability to inhibit Ena/VASP. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the subject-matter of claim 30.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims 76-79 have not been searched because the 'listeria motility domain' has not been defined in technical terms.

Claim 80 has not been searched because SEQ.ID.No.14 is not defined in the specification.

Claim 84 has not been searched because the composition has not been defined in technical terms.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/10249

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/10249

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0174378	A	11-10-2001	WO	0174378 A2	11-10-2001
WO 9801755	A	15-01-1998	WO	9801755 A1	15-01-1998
US 5990087	A	23-11-1999	US	5912128 A	15-06-1999